PROJECT TITLE: Gene Therapy for the Treatment of Malignant Brain Tumors with In Vivo Tumor Transduction with the Herpes Thymidine Kinase Gene/Ganciclovir System.

PRINCIPAL INVESTIGATORS: Corey Raffel, M.D., Ph.D. and Kenneth W. Culver, M.D.

NON-TECHNICAL ABSTRACT

The possibility of transferring a "sensitivity" gene into a growing brain tumor has been investigated. The purpose is to make the tumor sensitive to a type of chemotherapy that is relatively non-toxic to the rest of the body. The gene selected is the Herpes Simplex-thymidine kinase (HS-tk) gene. Herpes Simplex is a virus that can be killed by a drug called ganciclovir (GCV). By transferring the HS-tk gene into the tumor, using a disabled mouse virus called a "vector", the tumor will become like a herpes virus and the tumor can be killed with GCV.

Experiments in rats have shown that the direct injection of mouse cells producing a HS-tk vector into a growing brain tumor can result in complete destruction of the tumor with GCV therapy. We found no evidence of spread of the virus to the normal brain tissue or to other parts of the body. Based upon these findings, an initial trial is underway at the National Institutes of Health (NIH). To date eight people have been treated without evidence of toxicity. A second trial in adults has been approved. We now propose a human clinical trial for pediatric patients who are currently ineligible for treatment in the adult trials. In this study children with recurrent malignant brain tumors will be treated by injection of HS-tk vector-producer cells (VPC) into their tumors in an attempt to induce regression of the tumor with GCV therapy. The patient population consists of children who have failed standard therapy and have recurrent primary brain tumors with an expected survival of weeks to a few months.